IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

RONIN et al. Atty. Ref.: 1487-29; Confirmation No. 5743

Appl. No. 10/588,220 TC/A.U. 1644

Filed: April 17, 2008 Examiner: Huynh

For: PROCESS FOR SCREENING GLYCOFORM-SPECIFIC ANTIBODIES

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November 17, 2008

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE

Responsive to the Official Action dated September 17, 2008, the applicants elect, with traverse, the subject matter of the Examiner's Group I for further prosecution.

Reconsideration and withdrawal of the lack of unity objection and requirement for election are requested along with an early and favorable Action on the merits of all of the claimed subject matter for at least the reasons noted herein.

Unity of the subject matter of the Examiner's Groups I-IV

According to the Examiner's statement, processes of selecting antibodies that bind to different glycoproteins differ regarding the binding specificity, the glycosylation and/or branching state of the proteins TSH, LH, FSH and hCG. The Examiner is requested to appreciate however that TSH, LH, FSH and hCG hormones are dimeric peptides constituted by two subunits: the α-subunit and the β-subunit.

The α-subunit is a common subunit present in the four hormones, whereas the β-subunit is specific of the considered hormone. More specifically, TSH, LH, FSH and hCG share the same common α-subunit and have a specific βTSH subunit, βLH subunit, βFSH subunit and βhCG subunit, respectively.

Thus, the common link between the four above-mentioned hormones is the common α-subunit. A skilled person will appreciate that the α subunit is glycosylated, as well as the β-subunit.

Some antibodies directed against the α-subunit are disclosed in prior art (see for example the data sheet of FSHα subunit antibody attached hereto, which discloses the following in the paragraph “Applications”: “also recommended for the detection of TSH, LH and Gonadotropin α".

The applicants submit that from the teaching of the present application, an ordinarily skilled person will be able to carry out a process for screening antibodies directed against a first glycoprotein, comprising the step of the determination of binding between an antibody directed against a first glycoprotein (α-subunit), and at least one glycoform of a second glycoprotein, said second glycoprotein being itself a glycoform of the first glycoprotein.

Since the prior art does not discloses or suggest such a process, the technical feature of the invention should be considered as novel, and the lack of unity should be withdrawn. regarding the subject matter of the Examiner’s Groups I-IV. Withdrawal of the restriction requirement at least as between the subject matter of the Examiner’s Groups I-IV, and examination of the subject matter together, are requested.

Unity of the subject matter of the Examiner's Groups I and V-VIII

According to the Examiner's statement, the invention does not provide special technical features over Szudlinski et al. and the two documents of Papandreou et al.

According to the Examiner, a person of ordinary skilled would have screened antibodies directed against glycosylated recombinant TSH disclosed by Papandreou using the fucosylated/sialylated recombinant TSH disclosed by Szudlinski and the branching state disclosed by Papandreou

The applicants submit however that the present application discloses the use of antibodies able to recognize first "natural" glycosylated protein, in order to select antibodies able to interact with a second "recombinant" glycosylated protein wherein fucosylation, sialylation and branching states vary.

The applicants understand Papandreou et al (Mol and Cell. Endocrinology, 73 (1990) 15-26) to describe the study of TSH epitopes using specific monoclonal antibodies directed against α- and β-subunit of TSH. Fourteen (14) antibodies are able to interact with human TSH either partially or totally deglycosylated. There is no difference, regarding the interaction of the antibodies, between human TSH or deglycosylated TSH. It has also understood to have been shown in the paper of Papandreou et al that there exist epitopes named as α β heavily depend on the α subunit and are specific for TSH. Furthermore, it has been also shown that deglycosylation of β, but not α, subunit abolished the binding of anti TSH antibodies. These data have clearly indicated that the occupancy of glycosylation sites is

mandatory for antibody binding; this does not imply that antibodies are capable of recognizing to a variable extent TSH glycoforms which are glycosylated at the three sites with a variable degree of fucose, sialic acid or branching.

Thus, Papandreou et al. disclose that some epitope are dependant upon glycosylation states, the antibodies used in this document are able to interact with TSH with or without glycosylation. Moreover, Papandreou et al. does not teach that glycosylated form of second glycoprotein is fucosylated or sialylated.

Szudlinski et al. teach recombinant protein TSH fucosylated and/or sialylated. The sugar composition of the recombinant protein is determined by gas chromatography after the protein has been destroyed. However, Szudlinski et al does not teach the use of antibodies for detecting/analyzing the glycosylation state of said glycoprotein when it is in this intact form.

Papandreou et al (J Clin Endocrinol Metab. 1993 Aug;77(2):393-8) teach a process for determining the branching state of recombinant protein.

From the combination of the three documents cited by the Examiner, the applicants believe that one of ordinary skill in the art would not have found it obvious to have used antibodies for screening the branching state and the fucosylation/sialylation state of a recombinant protein. The cited art would not have led one of ordinary skill to have carried out a process for screening glycoform specific antibodies among antibodies elicited against a first glycoprotein, comprising a step of determination of the binding between antibodies elicited against a first glycoprotein, and at least one glycoform of a second glycoprotein, said second glycoprotein being itself a glycoform of

the first glycoprotein. As a consequence, the present application provides special technical features over the cited art, and therefore should be considered to form a single general inventive concept.

Withdrawal of the restriction requirement and an early and favorable Action on the merits of the claimed invention are requested.

The claims of the elected subject matter and the linking claims indicated by the Examiner read on the elected subject matter.

Rejoinder and allowance of any claim defining a method of making and/or using a product defined by an allowable claim, at an appropriate time, are requested.

Respectfully submitted,

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SANTA CRUZ BIOTECHNOLOGY, INC.

FSHα (BGN/F62/01): sc-80795

BACKGROUND

Follicle-stimulating hormone (FSH), also called follitropin, belongs to the family of glycoprotein hormones that also includes luteinizing hormone and thyroid-stimulating hormone. These hormones are secreted by the pituitary and exist as heterodimers, consisting of a common α subunit and a homologous but distinct β subunit. While the α subunit of FSH is involved in the binding of FSH to the receptor (follicle-stimulating hormone receptor, also known as FSHR), the β subunit stabilizes this interaction. This heterodimer regulates a variety of processes including secretion, posttranslational modification and signal transduction. Both FSH and FSHR are localized to Sertoli cells.

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RESEARCH USE

For research use only, not for use in diagnostic procedures.

CHROMOSOMAL LOCATION

Genetic locus: CGA (human) mapping to 6q15.

SOURCE

FSHα (BGN/F62/01) is a mouse monoclonal antibody raised against native FSHα of human origin.

PRODUCT

Each vial contains 100 µg IgG_1 in 1.0 ml of PBS with < 0.1% sodium azide and 0.1% gelatin.

APPLICATIONS

FSHα (BGN/F62/01) is recommended for detection of FSHα of human origin by solid phase ELISA (starting dilution 1:30, dilution range 1:30-1:3000); also recommended for the detection of TSH, LH and Gonadotropin α.

Suitable for use as control antibody for FSHα siRNA (h): sc-106976.

Molecular Weight of FSHα: 13 kDa.

STORAGE

Store at 4° C, **DO NOT FREEZE**. Stable for one year from the date of shipment. Non-hazardous. No MSDS required.

PROTOCOLS

See our web site at www.scbt.com or our catalog for detailed protocols and support products.